

such as, for example, Sybil/Base (Tripos, St. Louis, MO), Insight II (Molecular Simulations, San Diego, CA), and Sculpt (MDL Information Systems, San Leandro, CA)--.

In the Claims:

Amend claims 19 and 21 and add new claim 31 as indicated below.

19. (Amended) [The method of claim 18 further comprising] A method of identifying a compound which modulates activity of a target RNA comprising:

generating *in silico* a virtual library of compounds predicted or calculated to interact with a molecular interaction site within said RNA;

comparing three dimensional representations of said molecular interaction site with members of the virtual library of compounds to generate a hierarchy of said compounds ranked in accordance with their respective ability to form physical interactions with said molecular interaction site;

synthesizing the highly ranked members of said hierarchy of compounds; and

testing said highly ranked members to determine their ability to interact with said molecular interaction site by:

contacting the target RNA with at least one of said highly ranked members to provide a complex between the RNA and the member or members;

ionizing said complex;

fragmenting the ionized complex; and

determining whether highly ranked members bind to the molecular interaction site of said RNA.

21. (Amended) A method of identifying a compound which modulates activity of a target RNA comprising:

identifying at least one molecular interaction site on said target RNA, wherein said target RNA comprises single-stranded RNA and is mRNA, pre-mRNA, tRNA, rRNA, or snRNA;

generating *in silico* a virtual library of compounds predicted or calculated to interact with said molecular interaction site; and

comparing three dimensional representation of said molecular interaction site with members of the virtual library of compounds to generate a hierarchy of said compounds ranked in accordance with their respective ability to form physical interactions with said molecular interaction site.

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--31. A method of identifying a compound which modulates activity of a target RNA comprising:
identifying at least one molecular interaction site on said target RNA by comparing the nucleotide sequence of said target RNA with the nucleotide sequence of RNA from a different taxonomic species, identifying at least one conserved region, and determining the secondary structure of said conserved region, wherein said target RNA comprises single-stranded RNA and is mRNA, pre-mRNA, tRNA, rRNA, or snRNA;

generating *in silico* a virtual library of compounds predicted or calculated to interact with said molecular interaction site; and

comparing three dimensional representation of said molecular interaction site with members of the virtual library of compounds to generate a hierarchy of said compounds ranked in accordance with their respective ability to form physical interactions with said molecular interaction site.--

REMARKS

Claims 1-5 and 17-30 are pending in the present application. Claims 19 and 21 have been amended. New claim 31 has been added. Upon entry of the present amendment, claims 1-5 and 17-31 will be pending.

Claim 19 has been amended in order to place it into independent form and incorporates the subject matter of claims 17 and 18 from which it originally depended. No new matter has been added.

Claim 21 has been amended to specify that the target RNA comprises single-stranded RNA, support for which can be found in the specification at, for example, page 41, lines 12-15 where non-limiting examples of possible secondary structural motifs of target RNAs are listed, including